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## THE EFFECT OF HYPOXIA, COLD AND EXERCISE ON HUMAN THERMOREGULATION

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NAVAL MEDICAL RESEARCH AND DEVELOPMENT COMMAND **BETHESDA, MARYLAND** 

# THE EFFECT OF HYPOXIA, COLD, AND EXERCISE ON HUMAN THERMOREGULATION

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Human subjects participated in this study after giving their free and informed consent. Investigators adhered to NAVHLTHRSCHCENINST 6500.2, 2 Aug 95, concerning the protection of human volunteers in medical research.

#### **Summary**

#### **Problem**

Cold is associated with altitude; the higher the altitude, the lower the ambient temperature. As the ambient temperature decreases, oxygen consumption  $(\dot{V}O_2)$  increases in humans at rest. Resting thermogenesis, or the ability of the body to create heat to maintain homeostasis, occurs, in part, by shivering. In some animal species (pigeons, rats, cats, dogs, and humans) shivering has been shown to be suppressed due to breathing oxygen  $(O_2)$  at or below 12%. Since most U.S. Marine Corps cold-weather training occurs at altitude (2700 m), it is important to evaluate the relationship between reduced  $O_2$  and thermogenesis during rest and moderate exercise. In a military environment, hypothermia will impede combat performance by rendering the hypothermic person ineffective to carry out his/her mission, and it will increase manpower demands by requiring attention from at least one other person.

#### **Objective**

The primary objective of this investigation was to determine if exposure to moderate cold  $(4.4^{\circ}\text{C})$  and decreased  $O_2$  tension  $(15\% O_2$ , simulating 2700 m) reduces the ability of the human body to shiver and to maintain core and skin temperatures during moderate exercise.

#### **Approach**

Eight male and two female U.S. Navy and U.S. Marines Corps personnel participated as subjects. Subjects reported to the laboratory on 2 separate days with at least 48 hr between the two trials. The testing protocol consisted of (1) 15 min at room temperature (23°C) and room air (20.9%  $O_2$  [N]); (2) cold-air exposure (4.4°C) for 120 min while inhaling N or 15%  $O_2$  (H) at 40% relative humidity, and (3) 10 min at room temperature (23°C) and N. During the 120-min cold exposure, subjects sat for 40 min, walked 3.0 mph for 40 min, then sat for 40 min. Measurements included rectal ( $T_{re}$ ), and mean-weighted skin temperatures ( $\tilde{T}_{sk}$ ), thermal sensation (TS), ratings of perceived exertion (RPE), heart rate (HR), oxygen uptake ( $\tilde{V}O_2$ ), carbon

dioxide production ( $\dot{V}CO_2$ ), respiratory exchange ratio (RER), blood oxygen saturation ( $S_aO_2$ ), and electromyograms (EMGs) on left midchest and left upper trapezius.

#### Results

All subjects shivered vigorously during N and H cold as observed by investigators, reported in TS, and measured by EMGs. RER increased from 0.92 to 1.10 in H and was maintained in N from 0.90 to 0.92. Also,  $S_aO_2$  decreased more under H than N, decreasing to 94.4% and 97.2% at min 40, and 91.3% and 94.1% at min 60 for H and N, respectively. Although changes occurred over time, no condition effect occurred for  $T_{re}$ ,  $\bar{T}_{sk}$ , EMGs,  $\dot{V}O_2$ ,  $\dot{V}CO_2$ , TS, or RPE. During exercise, HR increased with no condition effect.

#### Conclusion

Exposure to 4.4°C and decreased  $O_2$  tension (15%  $O_2$ , simulating 2700 m) while at rest and while walking 3.0 mph, does not decrease the ability of the human body to shiver.  $T_{re}$  and  $T_{sk}$  decreased during rest and moderate exercise. The reduction of inspired  $O_2$  to 15% during exercise did increase the RER. This increase indicates a higher anaerobic metabolism and a greater carbohydrate need. The decrease in  $S_aO_2$  indicates less  $O_2$  is being carried in the blood, resulting in a possible limitation in aerobic capacity. Therefore, thermoregulation during military missions conducted at altitudes up to 2700 m should not be affected adversely by the reduction in inspired  $O_2$ .

#### Introduction

For terrestrial environments, cold is associated with altitude; the higher the altitude, the lower the ambient temperature. As the cold stress increases, oxygen consumption  $(\dot{V}O_2)$  and heat production increase in humans at rest (LeBlanc, 1986; Reading, Roberts, Pozos, & Hodgdon, 1996; Robinson & Haymes, 1990; Tikuisis, Bell, & Jacobs, 1991). As cold stress increases,  $\dot{V}O_2$  and heat production rise. This rise in  $\dot{V}O_2$  and heat production is primarily due to shivering (Kleinebeckel & Klussmann, 1990). When hypoxia is added to cold at rest, less shivering and lower  $\dot{V}O_2$  in humans can occur. Controversy exists regarding the threshold altitude or oxygen  $(O_2)$  percentage at which shivering is reduced. Reading et al., (1996) reported no decrease in shivering during rest at 4.4°C, 15%  $O_2$ . A threshold level of 12%  $O_2$  (simulating an altitude of 4160 m) has been proposed for a reduction in shivering and  $\dot{V}O_2$  (Blatteis, 1971; Kottke, Phalen, Taylor, Visscher, & Evans, 1948).

Resting thermogenesis is a process by which the body attempts to maintain thermal homeostasis, and it occurs, in part, by shivering. In the cold, if shivering is suppressed or eliminated, core body temperature will continue to decline. If core body temperature is not restored to normal and continues to decline below 35°C, a person can become hypothermic and die. In a military environment, hypothermia will impede combat performance by rendering a combatant ineffective to carry out the mission, and it can reduce manpower availability by requiring attention from at least one other person. Therefore, maintenance of a stable core temperature during cold exposure at rest and during activity is of paramount importance to battle troop readiness.

In some animal species (pigeons, rats, cats, dogs, and humans) shivering has been shown to be suppressed when breathing air with O<sub>2</sub> at or below 12% (Barnas & Rautenberg, 1990; Gautier & Bonora, 1992; Gautier & Bonora, 1994; Gautier, Bonora, Schultz, & Remmers, 1987;

Gautier, Bonora, & Trinh, 1993; Hemingway & Birzis, 1956; Kottke et al., 1948). VO<sub>2</sub> was reported to decrease in humans, small mammals, rats, and cats breathing 12% O<sub>2</sub> or lower (Blatteis & Luther, 1974; Frappell, Lanthier, Baudinette, & Mortola, 1992; Gautier, Bonora, & Remmers, 1989; Gautier & Bonora, 1992; Gautier & Bonora, 1994; Gautier et al., 1993; Giesbrecht, Fewell, Megirian, Brant, & Reemers, 1994; Hemingway & Birzis, 1956; Kottke et al., 1948). However, shivering was not shown to be suppressed in cold-acclimatized miniature pigs breathing 10% O<sub>2</sub> (Blatteis & Gilbert, 1974).

In humans, the response to exposure of either environmental cold or reduced  $O_2$  tension is well known. However, the thermoregulatory response to the combined stressors is unclear. Movement of an individual from sea level to 3000 m decreases the blood oxygen saturation  $(S_aO_2)$  from 96.7% to 92.0% (Ramirez, Agosti, Bittle, Dietz, & Colice, 1992). This level of  $S_aO_2$  has been associated with decreases in both aerobic  $(\dot{V}O_2$  max) and anaerobic (lactate threshold) parameters (Koistinen, Takala, Martikkala, & Leppaluoto, 1995). This effect is more pronounced in the well-trained athlete (Terrados, 1992). Hypoxia has also been associated with decreases in both rectal  $(T_{re})$  and mean-weighted skin temperature  $(\bar{T}_{sk})$  in humans resting in a thermoneutral room (Cipriano & Goldman, 1975). At rest in a thermoneutral room, breathing 12%  $O_2$  for 90 min had no effect on heart rate (HR), systolic blood pressure, ventilation, respiratory exchange ratio (RER), blood lactate,  $T_{re}$ , or  $\dot{W}_2$  (Robinson & Haymes, 1990).

It has been reported that nonshivering thermogenesis was decreased at 3350 m to 4340 m (Blatteis & Luther, 1976) but glucose utilization increased during both rest and exercise at 4300 m (Brooks et al., 1991). Exposure to 0°C air reduced the RER of humans (Hurley & Haymes, 1982), suggesting reduced glucose use at this temperature. Cold and altitude have been shown to modify glucose and the RER, but in conflicting directions.

Since most U.S. Marine Corps cold-weather training occurs at altitude (2700 m), it is important to evaluate the relationship among reduced  $O_2$ , cold, and thermogenesis. In the present study, breathing 15%  $O_2$  was used to simulate the acute respiratory and metabolic effects of an altitude of 2700 m. The purpose of this investigation was to determine if exposure to moderate cold (4.4°C) and 15%  $O_2$  decreases the ability of the human body to shiver and to maintain  $T_{re}$  and  $\tilde{T}_{sk}$  at rest and during light to moderate exercise. It was hypothesized that cold-induced increases in  $\dot{V}O_2$  would be suppressed during hypoxia, and that shivering would be increased despite a decreased metabolic response. It was further hypothesized that, during exercise,  $T_{re}$  would be lower than during rest, despite the heat generated by working muscles.

#### Methods

Eight male and two female U.S. Navy and U.S. Marines Corps personnel participated as subjects. All measurements and methods were approved by the Naval Health Research Center and the Naval Medical Research and Development Command committees for the protection of human subjects.

Subjects were informed of the nature, purpose, and potential risks of the experimental procedures, and signed Informed Consent and Privacy Act statements, as required by NAVHLTHRSCHCENINST 6500.2. All subjects underwent medical screening, which included a medical history questionnaire, body composition assessment, and clearance to participate by a medical officer. For pregnancy detection, a urine sample was tested for the presence of human chorionic gonadotropin. The pregnancy test was given to female subjects as part of the medical screening and prior to the two trials. Height and weight were determined using stadiometry and an electronic scale. Body density was determined from skinfolds using the three-site equation of Jackson and Pollock (1978); the Siri equation (1961) was used to determine relative body fat.

#### **Experimental Protocol**

Subjects reported to the laboratory on 2 separate days with at least 48 hr between the two trials. The influence of circadian rhythms on body temperature was controlled by conducting each test at the same time of day. Experimental conditions were presented to each subject in a counterbalanced, single-blind design. All trials were conducted at 4.4°C, 40% relative humidity. The test protocol consisted of: (1) 15 min at room temperature (23°C) and room air (20.9% O<sub>2</sub> [N]) (2) cold-air exposure (4.4°C) for 120 min while inhaling N or medical grade 15% O<sub>2</sub> (H), and (3) 10 min at room temperature (23°C) and N. During the 120-min cold exposure, subjects wore a nasal-oral face mask and sat for 40 min, walked 3.0 mph for 40 min on a treadmill, then sat for 40 min. During the tests, each subject wore shorts, T-shirt, socks, and tennis shoes.

Upon arrival at the laboratory, body weight was recorded. Each subject then inserted a rectal thermistor to a depth of 20 cm beyond the anal sphincter. Skin thermistors were placed on the right side of the body on the midbiceps, midchest, front midthigh, and back midcalf. Electrodes for electromyograms (EMGs) were placed on the left pectoralis major and the left upper trapezius. A Polar Vantage XL monitor (Polar USA, Inc.; Stamford, CT) was used to measure HR.  $T_{re}$  was measured using sterile, disposable Sher-I-Temp® thermistors. Skin temperatures were measured using silver skin thermocouples held in place with Hy® tape. A Grant 1200 series (12-bit) Squirrel Meter/Logger (Grant; Cincinnati, OH) was used to record  $T_{re}$  and skin temperatures. An ME3000P data recording device (Woodway, Inc.; Minneapolis, MN) was used to record and store EMGs. The median power frequency (MPF) and amplitude using root mean square (RMS) were calculated from the EMGs. A 9-point thermal sensation (TS) scale (Bedford, 1936) was used to determine how cold the subject felt (8 = extremely hot, 4 = neutral, 0 = extremely cold).

Carbon dioxide production ( $\dot{V}CO_2$ ) and  $\dot{V}O_2$  were determined using open-circuit spirometry. Expired gas was collected for 1.5 min in a Collins 100-L plastic bag (Warren E. Collins; Braintree, MA) connected to a two-way valve. Expired gas was analyzed for  $O_2$  and carbon dioxide ( $CO_2$ ) using S-3A/I  $O_2$  and CD-3A  $CO_2$  analyzers (Ametek; Pittsburgh, PA), respectively. Expired gas volume was measured using a 120-L tissot wet spirometer (Warren E. Collins; Braintree, MA). Blood pressure was measured using a manual aneroid sphygmomanometer and stethoscope. An Ohmeda® pulse volume oximeter attached to the finger measured  $S_2O_2$ .

Throughout the study, HR,  $T_{re}$ , and skin temperatures were recorded every minute.  $T_{sk}$  was calculated as: 0.35 ( $T_{chest} + T_{biceps}$ ) + 0.15 ( $T_{thigh} + T_{calf}$ ) (Mitchell & Wyndham, 1969). Exhaled gas, ratings of perceived exertion (RPE) on the 15-point Borg scale (Borg, 1970), TS, and  $S_aO_2$  were measured 6 different times during each trial: resting baseline (seated) prior to cold exposure; min 40, 60, 80, 120 of cold exposure, and 10 min after cold exposure. The 120-min cold exposure was divided into 3 time segments of 40 min each. During the first and third segments, the subject sat in a chair; during the second segment, the subject walked 3.0 mph on a motorized treadmill. At the end of cold exposure, while remaining seated, the subject was wheeled (wheels were on the chair) out of the chamber and remained seated until the last measurement was taken.

#### Statistical Analysis

Data were analyzed using a two-way, repeated-measures analysis of variance. The alpha level was set at 0.05. When significant differences were found, a Neumann-Kuels post hoc analysis was conducted.

#### Results

The subjects' physical characteristics were:  $(\bar{X} \pm SD)$  weight = 73.8 ± 11.4 kg, height = 175.6 ± 11.7 cm, percent fat = 13.4 ± 5.2%, fat free mass = 64.2 ± 11.8 kg, and fat mass = 9.6 ± 3.1 kg. All subjects shivered vigorously during N and H cold exposures, as observed by investigators and measured on EMGs. All subjects reported feeling cold as indicated by TS. RER over time increased during H from 0.92 to 1.10 and was maintained during N from 0.90 to 0.92 (see Figure 1).  $S_aO_2$  decreased more during the H than the N condition (see Figure 2). Although changes occurred over time, no condition effect occurred for  $\bar{T}_{sk}$ ,  $T_{re}$ , EMGs (MPF, RMS),  $\dot{V}O_2$ ,  $\dot{V}CO_2$ , watts, TS, or RPE. HR increased during exercise with no condition effect.

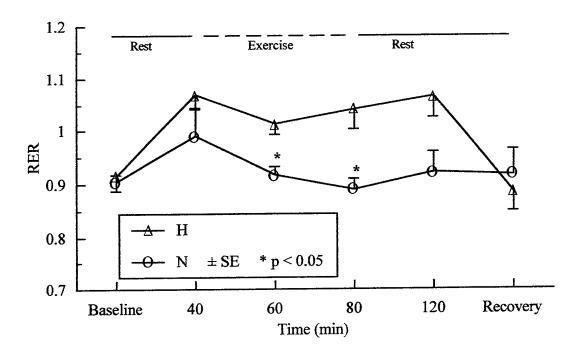


Figure 1. The respiratory exchange ratio for H and N, walking 3.0 mph from min 40 to 80.

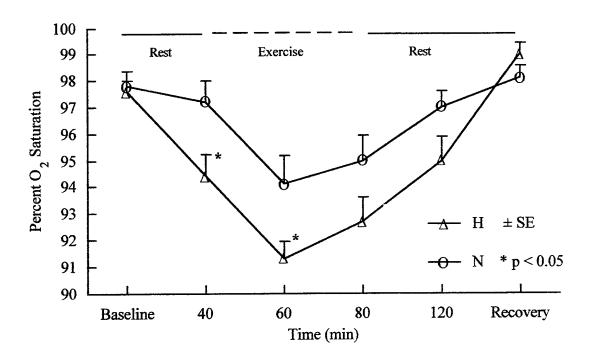


Figure 2. Blood oxygen saturation for H and N, walking 3.0 mph from min 40 to 80.

The  $\dot{V}O_2$  (see Figure 3) and  $\dot{V}CO_2$  analyses revealed no differences between the conditions (see Figure 4). The  $T_{re}$  (see Figure 5) and  $\bar{T}_{sk}$  (see Figure 6) analyses revealed no differences between the conditions. The TS and RPE analyses revealed no differences between the conditions. The HR analysis revealed no differences between the conditions (see Figure 7), and the watts analysis revealed no differences between the conditions (see Figure 8).

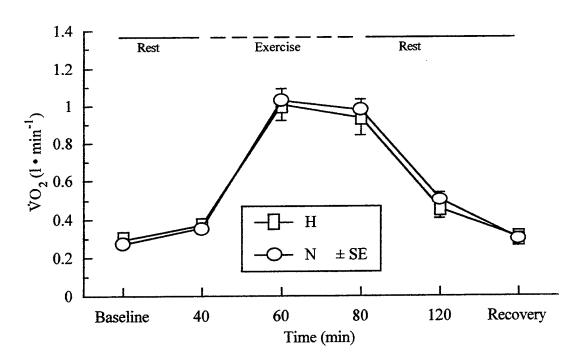


Figure 3. Oxygen consumption for H and N, walking 3.0 mph from min 40 to 80.

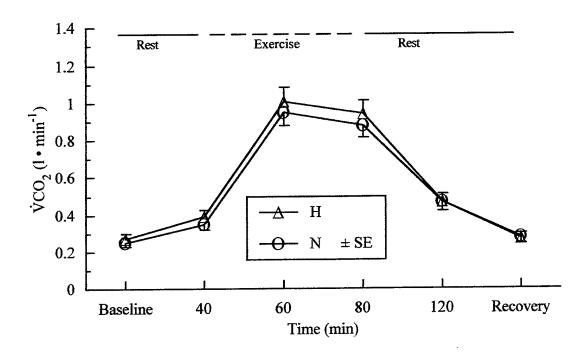


Figure 4. Carbon dioxide produced for H and N, walking 3.0 mph from min 40 to 80.

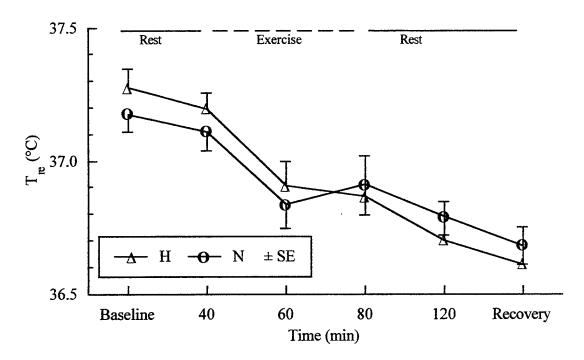


Figure 5. Rectal temperature for H and N, walking 3.0 mph from min 40 to 80.

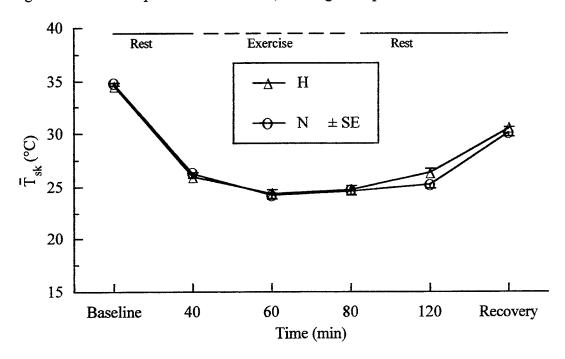


Figure 6. Mean-weighted skin temperature for H and N, walking 3.0 mph from min 40 to 80.

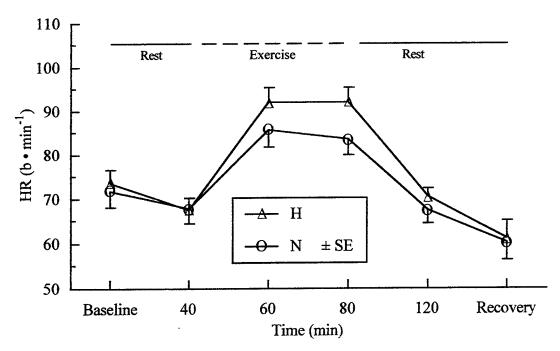


Figure 7. Heart rate for H and N, walking 3.0 mph from min 40 to 80.

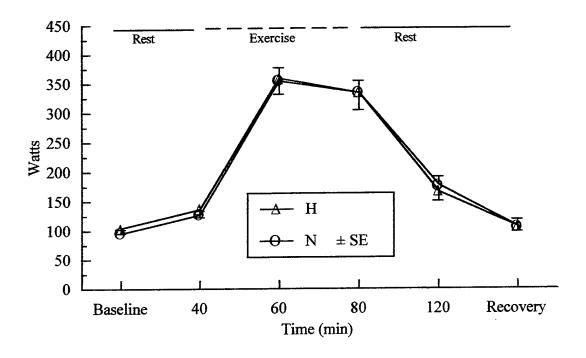


Figure 8. Watts for H and N, walking 3.0 mph from min 40 to 80.

No condition effect occurred for RMS or MPF. A gradual increase in RMS over time did occur in both conditions. Table 1 shows RMS and MPF values for both pectoralis major and trapezius muscles.

Table 1.  $Average \ (\pm \ SE) \ RMS \ (\mu V) \ and \ MPF \ (hz) \ Values \ for \ H \ and \ N \ for \ Pectoralis \ Major \ (Pec) \ and$   $Trapezius \ (Trap) \ Muscles$ 

Parameter	T= -10 min	T = 40 min	T = 60 min	T = 80 min	T = 120 min
Pec RMS H	$9.8 \pm 0.9$	$11.7 \pm 0.9$	$12.7 \pm 0.8$	$13.0 \pm 2.6$	16.4 ± 1.9
Pec RMS N	9.0 ± 1.2	$12.2 \pm 1.5$	$18.9 \pm 2.6$	$16.1 \pm 2.0$	14.2 ± 1.7
Trap RMS H	$4.1 \pm 0.5$	$7.9 \pm 2.8$	$47.8 \pm 6.4$	54.9 ± 11.5	$20.6 \pm 7.3$
Trap RMS N	$9.0 \pm 4.9$	$8.6 \pm 2.2$	$60.1 \pm 7.5$	$55.9 \pm 6.0$	$16.5 \pm 3.2$
Pec MPF H	4.1 ± 0.2	7.1 ± 1.5	7.4 ± 1.2	$8.6 \pm 2.2$	$10.6 \pm 1.7$
Pec MPF N	$6.2 \pm 2.0$	$10.6 \pm 2.2$	$9.6 \pm 1.8$	9.9 ± 1.6	11.9 ± 1.6
Trap MPF H	7.7 ± 1.7	9.6 ± 1.7	$8.5 \pm 0.7$	9.1 ± 1.1	14.7 ± 1.3
Trap MPF N	$8.8 \pm 1.9$	12.9 ± 1.4	$8.8 \pm 1.2$	7.6 ± 1.2	$16.3 \pm 1.3$

#### **Discussion**

It has been proposed that breathing  $O_2$  at concentrations of 12% (4160 m) or lower has significant effects on human thermoregulation during a prolonged cold stress (Blatteis, 1971; Kottke et al., 1948). Within the U.S. military training environment, exposure to altitudes of

2700 m to 3000 m is routine, but those above 3000 m are much less frequent. Therefore, the U.S. military needs to evaluate exposure to moderate altitude (reduced  $O_2$  tension) and its effect on thermoregulation in humans.

In the present study, exercise thermogenesis appeared to override any decrement in shivering thermogenesis. The cold stress was sufficient to cause shivering thermogenesis to begin, and the effects of the reduction in inspired  $O_2$  were not large enough to reduce the shivering thermogenesis. The increase in thermogenesis due to shivering and exercise was insufficient to maintain  $T_{re}$  and  $\tilde{T}_{sk}$  over the duration of the experiment, since the trend was downward over the duration of the exposure.

The subjects in this study were in an artificial situation (sitting quietly or walking on a treadmill in a cold environment while lightly dressed) so the decrease in  $T_{re}$  might not be a factor if normal thermal protective clothing were worn. Shivering was not suppressed while  $\tilde{T}_{sk}$  and  $T_{re}$  were decreasing during rest and light to moderate exercise.

#### Conclusion

The reduction of inspired  $O_2$  from 20.9% to 15% during exercise resulted in an increase in RER. This increase indicates a higher anaerobic metabolism and a greater need for carbohydrates (glucose) in food. The decrease in  $S_aO_2$  indicates less oxygen is being carried in the blood, resulting in a possible limitation in aerobic capacity. Therefore, thermoregulation during military missions conducted at altitudes up to 2700 m should not be affected adversely by the reduction in inspired  $O_2$ .

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U.S. Marine and Navy personnel may be at an increased risk for developing hypothermia when training at 2700 m. The objective of this study was to determine if exposure to moderate cold and decreased oxygen (O <sub>2</sub> ) tension (15% O <sub>2</sub> simulating 2700 m) reduces the ability of the human body shiver and to maintain core and skin temperatures during moderate exercise. Eight male and two female U.S. Navy and Marine Corps personnel participated as subjects. Subjects were exposed to 4.4° C air breathing either 20.9% O <sub>2</sub> (N) or 15% O <sub>2</sub> (H) for 120 min, 40 min sitting, then 40 min walking on a treadmill at 3.0 mph, then sitting for 40 min. All subjects shivered vigorously during and H cold as observed by investigators, reported in thermal sensation, and measured by electromyograms. The exposure of H does not decrease the ability of the human body to shiver. The respiratory exchange ratio did increase with H, indicating an increased need for glucose, and H decreased the O <sub>2</sub> blood saturation, indicating less O <sub>2</sub> is being carried in the blood, resulting in a possible limitation in maximal aerobic capacity. Therefore, thermoregulation during military mission conducted at altitudes up to 2700 m should not be affected adversely by the reduction in inspired C	N H	
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